Amendments to the Specification

Please amend the paragraph beginning at page 15, line 14, as follows:

As noted, the invention further embraces the treatment of solid, non-lymphoid tumors by the administration of an anti-cytokine antibody, e.g., an anti-IL10 antibody, and a B cell specific antibody, preferably an antibody having substantial B cell depleting activity such as RITUXAN® (rituximab). It ahs been reported that some solid tumors apparently have B cell involvement. That is to say that the B cells are somehow involved in promoting or maintaining the tumorigenic state and may impede the body's immune defense system against such tumor. With respect thereto, WO 020864 A1, incorporated by reference herein, which identifies Biocrystal Inc. as the Applicant describes the treatment of solid, non-lymphoid tumor using antibodies that target B cells, including ~~Rituxan®~~ RITUXAN® (rituximab). It was reported therein that this treatment resulted in pronounced anti-tumor responses, even in patients with advanced colorectal cancer, lung cancer and liver cancer.

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Please amend the paragraph beginning at page 15, line 29, as follows:

This combination regimen should afford an enhanced method of treating solid tumors, particularly those wherein B cells are involved, but are not themselves the cancerous cells. In this regimen, the cytokine antagonist, e.g., anti-cytokine antibody and the B cell depleting antibody, e.g., ~~Rituxan®~~ RITUXAN® (rituximab) will be administered separately or together and in either order.

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Please amend the paragraph beginning at page 25, line 21, as follows:

Examples of antibodies which bind the CD20 antigen include: "C2B8" which is now called "rituximab" ("RITUXAN®") (US Patent No. 5,736,137, expressly incorporated herein by reference); the yttrium-[90]-labeled 2138 murine antibody designated "Y2B8" (US Patent No. 5,736,137, expressly incorporated herein by reference); murine IgG2a "131" optionally labeled with 1311 to generate the "131I-B1" antibody (BEXXARTM®) (US Patent No. 5,595,721, expressly incorporated herein by reference); murine monoclonal antibody "1F5" (Press *et al. Blood* 69(2):584-591 (1987)); "chimeric 2H7" antibody (US Patent No. 5,677,180, expressly incorporated herein by reference); and monoclonal antibodies L27, G28-2, 93-1133, B-Cl or NU-B2 available from the International Leukocyte Typing Workshop (Valentine *et al.*, In: *Leukocyte Typing III* (McMichael, Ed., p. 440, Oxford

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University Press (1987)). Examples of antibodies which bind the CD19 antigen include the anti-CD 19 antibodies in Hekman *et al., Cancer Immunol. Immunother.* 32:364-372 (1991) and Vlasveld *et al. Cancer Immunol. Immunother.* 40:37-47(1995); and the B4 antibody in Kiesel *et al. Leukemia Research 11,* 12: 1119 (1987).

Please amend the paragraph beginning at page 28, line 5, as follows:

A "chemotherapeutic agent" is a chemical compound useful in the treatment of cancer. Examples of chemotherapeutic agents include alkylating agents such as thiotepa and cyclosphosphamide (CYTOXANTM®); alkyl sulfonates such as busulfan, improsulfan and piposulfan; aziridines such as benzodopa, carboquone, meturedopa, and uredopa; ethylenimines and methylamelamines including altretamine, triethylenemelamine, trietylenephosphoramide, triethylenethiophosphaoramide and trimethylolomelamine; nitrogen mustards such as chlorambucil, chlornaphazine, cholophosphamide, estramustine, ifosfamide, mechlorethamine, mechlorethamine oxide hydrochloride, melphalan, novembiehin, phenesterine, prednimustine, trofosfamide, uracil mustard; nitrosureas such as carmustine, chlorozotocin, fotemustine, lomustine, nimustine, ranimustine; antibiotics such as aclacinomysins, actinomycin, authramycin, azaserine, bleomycins, cactinomycin, calicheamicin, carabicin, carminomycin, carzinophilin, chromoinycins, dactinomycin, daunorubicin, detorubicin, 6-diazo-5-oxo-L-norleucine, doxorubicin, epirubicin, esorubicin, idambicin, marcellomycin, mitomycins, mycophenolic acid, nogalamycin, olivomycins, peplomycin, potfiromycin, puromycin, quelamycin, rodorubicin, streptonigrin, streptozocin, tubercidin, ubenimex, zinostatin, zorubicin; anti-metabolites such as methotrexate and 5-fluorouracil (5-FU); folic acid analogues such as denopterin, methotrexate, pteropterin, trimetrexate; purine analogs such as fludarabine, 6-mercaptopurine, thiamiprine, thioguanine; pyrimidine analogs such as ancitabine, azacitidine, 6-azauridine, carmofur, cytarabine, dideoxyuridine, doxifluridine, enocitabine, floxuridine, 5-FU; androgens such as calusterone, dromostanolone propionate, epitiostanol, mepitiostane, testolactone; anti-adrenals such as aminoglutethimide, mitotane, trilostane; folic acid replenisher such as frolinic acid; aceglatone; aldophosphamide glycoside; aminolevulinic acid; amsacrine; bestrabucil; bisantrene; edatraxate; defofamine; demecolcine; diaziquone; elfornithine; elliptinium acetate; etoglucid; gallium nitrate; hydroxyurea; lentinan; lonidamine; mitoguazone; mitoxantrone; mopidamol; nitracrine; pentostatin; phenamet; pirarubicin; podophyllinic acid; 2-ethylhydrazide; procarbazine; PSK®; razoxane; sizofrran; spirogermanium; tenuazonic acid;

triaziquone; 2, 2',2"-trichlorotriethylamine; urethan; vindesine; dacarbazine; mannomustine; mitobronitol; mitolactol; pipobroman; gacytosine; arabinoside ("Ara-C"); cyclophosphamide; thiotepa; taxoids, e.g. paclitaxel (TAXOLO, Bristol-Myers Squibb Oncology, Princeton, NJ) and doxetaxel (TAXOTEW, Rh6ne-Poulenc Rorer, Antony, France); chlorambucil; gemcitabine; 6-thioguanine; mercaptopurine; methotrexate; platinum analogs such as cisplatin and carboplatin; vinblastine; platinum; etoposide (VP-16); ifosfamide; mitomycin C; mitoxantrone; vincristine; vinorelbine; navelbine; novantrone; teniposide; daunomycin; aminopterin; xeloda; ibandronate; CPT-11; topoisomerase inhibitor RFS 2000; difluoromethylornithine (DMFO); retinoic acid; esperamicins; capecitabine; and pharmaceutically acceptable salts, acids or derivatives of any of the above. Also included in this definition are anti-hormonal agents that act to regulate or inhibit hormone action on tumors such as anti-estrogens including for example tamoxifen, raloxifene, aromatase inhibiting 4(5)-imidazoles, 4 hydroxytamoxifen, trioxifene, keoxifene, LY117018, onapristone, and toremifene (Fareston); and anti-androgens such as flutamide, nilutamide, bicalutamide, leuprolide, and goserelin; and pharmaceutically acceptable salts, acids or derivatives of any of the above.

Please amend the paragraph beginning at page 52, line 22, as follows:

A composition comprising an antagonist which binds to a B cell surface antigen and a composition which contains a cytokine antagonist, e.g. an antibody, wherein both may be in the same composition will be formulated, dosed, and administered in a fashion consistent with good medical practice. Preferably, the anti-cytokine will comprise an anti-IL10 antibody and the B cell antagonist will comprise a B cell depleting antibody, preferably an anti-CD20 antibody such as ~~Rituxan®~~ RITUXAN® (rituximab). Factors for consideration in this context include the particular disease or disorder being treated, the particular mammal being treated, the clinical condition of the individual patient, the cause of the disease or disorder, the site of delivery of the agent, the method of administration, the scheduling of administration, and other factors known to medical practitioners. The therapeutically effective amount of the antagonist to be administered will be governed by such considerations.

Please amend the paragraph beginning at page 53, line 8, as follows:

The preferred antagonist is an antibody, e.g. an antibody such as RITUXAN® (rituximab), which is not conjugated to a cytotoxic agent. Suitable dosages for an

unconjugated antibody are, for example, in the range from about 20mg/~~mz~~m2 to about 1000mgm2. In one embodiment, the dosage of the antibody differs from that presently recommended for RITUXAN® (rituximab). For example, one may administer to the patient one or more doses of substantially less than 375mg/m2 of the antibody, *e.g.* where the dose is in the range from about 20mg/mz to about 250mg/m2, for example from about 50mg/m2 to about 200mg/m2.

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Please amend the paragraph beginning at page 56, line 18, as follows:

A patient with non-Hodgkin's lymphoma is intravenously administered an anti-IL10 antibody at a dosage of 50mg/m^2 IV weekly for four weeks. Thereafter, the patient is administered RITUXAN® (rituximab) intravenously according to the following dosage schedules:

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(A) 50mg/m^2 IV day 1
150mg/m^2 IV days on 8, 15 & 22

(B) 150mg/m^2 IV day 1
375mg/m^2 IV on days 8, 15 & 22

(C) 375mg/m^2 IV on days 1, 8, 15 & 22

This same patient is administered CHOP chemotherapy according to the regimen described in US Patent 5,736,137.

Please amend the paragraph beginning at page 57, line 4, as follows:

A patient having an advanced colorectal cancer characterized by B cell involvement is treated concurrently with an anti-IL10 antibody and RITUXAN® (rituximab) at the same dosages as in Example 1.

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Please amend the paragraph beginning at page 69, line 10, as follows:

The invention also provides combination therapies for solid tumors having B cell involvement comprising the administration of an anti-cytokine antibody and a B cell depleting antibody such as RITUXAN® (rituximab).

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